Patent Claims

1. Compounds of the formula I

5		X-Ar
10		z N
	in which	
	Ar	denotes phenyl, naphthyl, biphenyl or Het, each of
15		which is unsubstituted or mono-, di-, tri-, tetra- or penta- substituted by R ¹ ,
15	X	denotes -O-, -S-, -(CH ₂) _n -, -C(=O)-, -CH(OH)-, -(CH ₂) _n O-,
		$-O(CH_2)_{n^-}$, $-(CH_2)_nS$, $-S(CH_2)_{n^-}$, $-(CH_2)_nNH$, $-NH(CH_2)_{n^-}$,
		-(CH ₂) _n NA-, -NA(CH ₂) _n -, -CHHal- or -C(Hal) ₂ -,
20	Υ	denotes O, S, CH-NO ₂ , C(CN) ₂ or N-R ⁴ ,
	Z	denotes -Ar, -Ar-X-Ar, -CH ₂ -Ar or -CH ₂ -Ar-X-Ar,
	Het	denotes a mono- or bicyclic aromatic heterocycle having 1 to 4 N, O and/or S atoms,
25	R^1	denotes A, Ar', OR ³ , SR ³ , OAr', SAr', N(R ³) ₂ , NHAr', Hal,
		NO_2 , CN , $(CH_2)_mCOOR^3$, $(CH_2)_mCON(R^3)_2$, COR^3 ,
		S(O) _m A, S(O) _m Ar', NHCOA, NHCOAr', NHSO ₂ A,
		$NHSO_2Ar'$, $SO_2N(R^3)_2$, $-O-(CH_2)_p-NH_2$, $-O-(CH_2)_p-NHA$,
20		$-O-(CH_2)_p-NA_2$, $-NH-(CH_2)_p-NH_2$, $-NH-(CH_2)_p-NHA$,
30		$-NH-(CH_2)_p-NA_2$, $-NA-(CH_2)_p-NH_2$, $-NA-(CH_2)_p-NHA$,
		-NA- $(CH_2)_p$ -NA ₂ , -O- $(CH_2)_n$ -Het ¹ or Het ¹ ,
	R^3	denotes H, A or -(CH ₂) _n Ar',
	R⁴	denotes H, CN, OH, A, (CH ₂) _m Ar', COR ³ , COAr', S(O) _m A
35		or S(O) _m Ar',

		Ar'	denotes phenyl which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by A, Ph, OH, OA, SH, SA,
			OPh, SPh, NH ₂ , NHA, NA ₂ , NHPh, Hal, NO ₂ , CN, (CH ₂) _m COOH, (CH ₂) _m COOH ₂ ,
5			$(CH_2)_mCONHA$, CHO , COA , $S(O)_mA$, $S(O)_mPh$, $NHCOA$,
			NHCOPh, NHSO ₂ A, NHSO ₂ Ph or SO ₂ NH ₂ ,
		Ph	denotes phenyl which is unsubstituted or mono-, di- or
		• • • •	trisubstituted by A, Hal, CN, COOR, COOH, NH ₂ , NO ₂ ,
10			OH or OA,
		Het ¹	denotes a monocyclic saturated heterocycle having 1 to
		1100	4 N, O and/or S atoms, which may be unsubstituted or
			mono-, di- or trisubstituted by Hal, A, OA, CN,
45			$(CH_2)_nOH$, $(CH_2)_nHal$, NH_2 , $=NH$, $=N-OH$, $=N-OA$ and/or
15			carbonyl oxygen (=O),
		Α	
		^	denotes alkyl having 1 to 10 C atoms, in which, in addition 1.7 H stamp may be replaced by 5 and/ar ablasia.
		Цаі	tion, 1-7 H atoms may be replaced by F and/or chlorine,
20		Hal	denotes F, Cl, Br or I,
		n	denotes 0, 1, 2 or 3,
		m 	denotes 0, 1 or 2,
		p	denotes 1, 2, 3 or 4,
25			ceutically usable derivatives, solvates, salts and stereo-
23		isomers ther	eof, including mixtures thereof in all ratios.
	2.	Compounds	according to Claim 1, in which
		X	denotes O or -(CH ₂) _n -,
30		and pharma	ceutically usable derivatives, solvates, salts and stereo-
		isomers ther	eof, including mixtures thereof in all ratios.
	3.	Compounds	according to Claim 1 or 2, in which
25		Ar	denotes Het or phenyl, each of which is unsubstituted or
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mono-, di-, tri-, tetra- or pentasubstituted by R^1 ,

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and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.

4. Compounds according to one or more of Claims 1-3, in which R^1 denotes A, OH, OA, NH₂, NHA, NA₂, HaI, $(CH_2)_mCONH_2$, $(CH_2)_mCONHA$, $(CH_2)_mCONA_2$, $-O-(CH_2)_p-NH_2$, $-O-(CH_2)_p-NHA$, $-O-(CH_2)_p-NA_2$, $-NH-(CH_2)_p-NH_2$, $-NH-(CH_2)_p-NH_2$, $-NH-(CH_2)_p-NH_2$, $-NA-(CH_2)_p-NHA$, $-NA-(CH_2)_p-NHA$, $-NA-(CH_2)_p-NA_2$, $-O-(CH_2)_n-Het^1$ or Het^1 ,

and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.

- Compounds according to one or more of Claims 1-4, in which
 Het denotes a monocyclic aromatic heterocycle having 1 to 3 N, O and/or S atoms,
- and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.
 - Compounds according to one or more of Claims 1-5, in which
 Y denotes O,
 and pharmaceutically usable derivatives, solvates, salts and stereo-isomers thereof, including mixtures thereof in all ratios.
- Compounds according to one or more of Claims 1-6, in which
 Z denotes -Ar,
 and pharmaceutically usable derivatives, solvates, salts and stereo-isomers thereof, including mixtures thereof in all ratios.
 - 8. Compounds according to one or more of Claims 1-7, in which

5			denotes phenyl which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by A, OH, OA, NH ₂ , NHA, NA ₂ , -O-(CH ₂) _p -NH ₂ , -O-(CH ₂) _p -NHA, -O-(CH ₂) _p -NA ₂ , -NH-(CH ₂) _p -NH ₂ , -NH-(CH ₂) _p -NHA, -NH-(CH ₂) _p -NA ₂ , -NA-(CH ₂) _p -NH ₂ , -NA-(CH ₂) _p -NHA, -NA-(CH ₂) _p -NA ₂ , -O-(CH ₂) _n -Het ¹ or Het ¹ or Hal, naceutically usable derivatives, solvates, salts and stereoereof, including mixtures thereof in all ratios.
9. Compounds according to one or more of Claims 1-8, i		ds according to one or more of Claims 1-8, in which	
		X	denotes O,
15		Ar	denotes Het or phenyl, each of which is unsubstituted or
			mono-, di-, tri-, tetra- or pentasubstituted by R ¹ ,
		R^1	denotes A, OH, OA, NH ₂ , NHA, NA ₂ , Hal, -O-(CH ₂) _p -NH ₂ ,
			$-O-(CH_2)_p-NHA$, $-O-(CH_2)_p-NA_2$, $-NH-(CH_2)_p-NH_2$,
			-NH-(CH ₂) _p -NHA, -NH-(CH ₂) _p -NA ₂ , -NA-(CH ₂) _p -NH ₂ ,
20			-NA-(CH ₂) _p -NHA, -NA-(CH ₂) _p -NA ₂ , (CH ₂) _m CONH ₂ ,
20			$(CH_2)_mCONHA$, $(CH_2)_mCONA_2$, $-O-(CH_2)_n-Het^1$ or Het^1
		Het	denotes a monocyclic aromatic heterocycle having 1 to 3
			N, O and/or S atoms,
		Het ¹	denotes a monocyclic saturated heterocycle having 1 to 2
25			N and/or O atoms, which may be unsubstituted or
			monosubstituted by A or (CH ₂) _n OH,
		Υ	denotes O,
		Z	denotes -Ar,
30		Α	denotes alkyl having 1 to 10 C atoms, in which, in addi-
			tion, 1-7 H atoms may be replaced by F and/or chlorine,
		Hal	denotes F, Cl, Br or I,
35		m	denotes 0, 1 or 2,
		р	denotes 1, 2, 3 or 4,
			aceutically usable derivatives, solvates, salts and stereo-
		isomers the	ereof, including mixtures thereof in all ratios.

	10.	Compounds according to one or more of Claims 1-9, in which	
		X	denotes O,
_		Ar	denotes Het which is unsubstituted or mono-, di- or
5			trisubstituted by R ¹ ,
		R^1	denotes $(CH_2)_mCONH_2$, $(CH_2)_mCONHA$ or $(CH_2)_mCONA_2$,
		Het	denotes furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxa-
			zolyl, thiazolyl, pyridyl, pyrimidinyl, pyridazinyl or pyraz-
10			inyl,
		Het ¹	denotes a monocyclic saturated heterocycle having 1 to 2
			N and/or O atoms, which may be unsubstituted or
			monosubstituted by A or (CH ₂) _n OH,
15		Υ	denotes O,
		Z	denotes phenyl which is unsubstituted or mono-, di-, tri-,
			tetra- or pentasubstituted by A, OH, OA, NH ₂ , NHA, NA ₂ ,
			$-O-(CH_2)_p-NH_2$, $-O-(CH_2)_p-NHA$, $-O-(CH_2)_p-NA_2$,
20			-NH- $(CH_2)_p$ -NH ₂ , -NH- $(CH_2)_p$ -NHA, -NH- $(CH_2)_p$ -NA ₂ ,
			$-NA-(CH_2)_p-NH_2$, $-NA-(CH_2)_p-NHA$, $-NA-(CH_2)_p-NA_2$,
			-O-(CH ₂) _n -Het ¹ or Het ¹ or Hal,
		Α	denotes alkyl having 1 to 10 C atoms, in which, in addi-
25			tion, 1-7 H atoms may be replaced by F and/or chlorine,
23		Hal	denotes F, Cl, Br or I,
		m	denotes 0, 1 or 2,
		p	denotes 1, 2, 3 or 4,
			aceutically usable derivatives, solvates, salts and stereo-
30		isomers the	ereof, including mixtures thereof in all ratios.
	11.	Compound	s according to one or more of Claims 1-10, in which
35		Ar	denotes phenyl, naphthyl, biphenyl or Het, each of which
			is unsubstituted or mono-, di-, tri-, tetra- or pentasubsti-
			tuted by R ¹ ,
		X	denotes -O- or - $(CH_2)_{n-1}$

		Υ	denotes O,
		Z	denotes phenyl which is unsubstituted or mono-, di-, tri-,
			tetra- or pentasubstituted by R ¹ , -phenylene-X-Ar, -CH ₂ -
			Ar or -CH ₂ -phenylene-X-Ar,
5		Het	denotes a monocyclic aromatic heterocycle having 1 to 3
			N, O and/or S atoms,
		Het ¹	denotes a monocyclic saturated heterocycle having 1 to 2
			N and/or O atoms, which may be unsubstituted or mono-
10			substituted by A or (CH ₂) _n OH,
		R ¹	denotes A, OH, OA, NH ₂ , NHA, NA ₂ , Hal, (CH ₂) _m CONH ₂ ,
			$(CH_2)_mCONHA$, $(CH_2)_mCONA_2$, $S(O)_mA$, $-O-(CH_2)_p-NH_2$,
			$-O-(CH_2)_p-NHA$, $-O-(CH_2)_p-NA_2$, $-NH-(CH_2)_p-NH_2$,
15			-NH-(CH ₂) _p -NHA, -NH-(CH ₂) _p -NA ₂ , -NA-(CH ₂) _p -NH ₂ ,
			-NA-(CH ₂) _p -NHA, -NA-(CH ₂) _p -NA ₂ , -O-(CH ₂) _n -Het ¹ or Het ¹
		Α	denotes alkyl having 1 to 10 C atoms, in which, in addi-
			tion, 1-7 H atoms may be replaced by F and/or chlorine,
20		Hal	denotes F, Cl, Br or I,
20		n	denotes 0, 1, 2 or 3,
		m	denotes 0, 1 or 2,
		р	denotes 1, 2, 3 or 4,
		and pharm	aceutically usable derivatives, solvates, salts and stereo-
25		isomers the	ereof, including mixtures thereof in all ratios.
	12.	Compound	s according to Claim 1, selected from the group
30		<i>N</i> -met	thyl-4-{4-[5-(4-chloro-3-trifluoromethylmethylphenyl-
		carbamoyl)	-1 <i>H</i> -pyrrol-3-yl]phenoxy}pyridine-2-carboxamide,
			thyl-4-{3-[5-(4-chloro-3-trifluoromethylmethylphenyl-
		carbamoyl)	-1 <i>H</i> -pyrrol-3-yl]phenoxy}pyridine-2-carboxamide,

N-methyl-4-{4-[5-(3-chloro-4-methylphenylcarbamoyl)-1H-pyrrol-

3-yl]phenoxy}pyridine-2-carboxamide,

N-methyl-4-{4-[5-(2-methoxy-5-trifluoromethylphenylcarbamoyl)-1*H*-pyrrol-3-yl]phenoxy}pyridine-2-carboxamide, N-methyl-4-{3-[5-(3-chloro-4-methylmethylphenylcarbamoyl)-1Hpyrrol-3-yl]phenoxy}pyridine-2-carboxamide, 5 N-methyl-4-{4-[5-(3-chloro-6-methoxymethylphenylcarbamoyl)-1*H*-pyrrol-3-yl]phenoxy}pyridine-2-carboxamide, N-methyl-4-{3-[5-(3-chloro-6-methoxymethylphenylcarbamoyl)-1*H*-pyrrol-3-yl]phenoxy}pyridine-2-carboxamide, 10 N-methyl-4-{3-[5-(2-methoxy-5-trifluoromethylmethylphenylcarbamoyl)-1*H*-pyrrol-3-yl]phenoxy}pyridine-2-carboxamide, N-methyl-4-{3-[5-(2,5-dimethoxy-4-chlorophenylcarbamoyl)-1Hpyrrol-3-yl]phenoxy}pyridine-2-carboxamide. N-methyl-4-{3-[5-(4-bromo-3-trifluoromethylphenylcarbamoyl)-15 1*H*-pyrrol-3-yl]phenoxy}pyridine-2-carboxamide. N-methyl-4-{3-[5-(3-trifluoromethoxyphenylcarbamoyl)-1Hpyrrol-3-yl]phenoxy}pyridine-2-carboxamide. N-methyl-4-{3-[5-(4-tert-butylphenylcarbamoyl)-1H-pyrrol-3-yl]-20 phenoxy)pyridine-2-carboxamide. N-methyl-4-{3-[5-(3,4-dichlorophenylcarbamoyl)-1H-pyrrol-3-yl]phenoxy}pyridine-2-carboxamide, N-methyi-4-{3-[5-(4-chloro-3-methyl-6-25 methoxyphenylcarbamoyl)-1H-pyrrol-3-yl]phenoxy}pyridine-2-carboxamide. N-methyl-4-{3-[5-(2,4-dimethoxy-5-trifluoromethoxyphenylcarbamoyl)-1*H*-pyrrol-3-yl]phenoxy}pyridine-2-carboxamide, 30 N-methyl-4-{3-[5-(2-dimethylamino-5-trifluoromethylphenylcarbamoyl)-1*H*-pyrrol-3-yl]phenoxy}pyridine-2-carboxamide. N-methyl-4-{3-[5-(2-(2-methylaminoethoxy)-5-methylphenylcarbamoyl)-1*H*-pyrrol-3-yl]phenoxy}pyridine-2-carboxamide. N-methyl-4-{3-[5-(2-(2-dimethylaminoethoxy)-5-methylphenyl-35 carbamoyl)-1*H*-pyrrol-3-yl]phenoxy}pyridine-2-carboxamide,

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N-methyl-4-{3-[5-(2-[(2-dimethylaminoethyl)methylamino]-5-methylphenylcarbamoyl)-1*H*-pyrrol-3-yl]phenoxy}pyridine-2-carboxamide,

- and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.
- 13. Process for the preparation of compounds of the formula I according to Claims 1-10 and pharmaceutically usable derivatives, salts, solvates and stereoisomers thereof, characterised in that
 - a) for the preparation of compounds of the formula I in which Y denotes O,
 - a compound of the formula II

in which X and Ar have the meanings indicated in Claim 1, and L denotes Cl, Br, I or a free or reactively functionally modified OH group,

is reacted with a compound of the formula III

Z-NH₂ III

in which Z has the meaning indicated in Claim 1,

and/or

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a base or acid of the formula I is converted into one of its salts.

- 14. Medicaments comprising at least one compound of the formula I according to Claim 1 and/or pharmaceutically usable derivatives, salts, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and optionally excipients and/or adjuvants.
- 15. Use of compounds according to Claim 1
 and pharmaceutically usable derivatives, salts, solvates and stereoisomers thereof, including mixtures thereof in all ratios,
 for the preparation of a medicament for the treatment of diseases
 in which the inhibition, regulation and/or modulation of kinase signal
 transduction plays a role.
 - 16. Use according to Claim 15, which involves Raf kinase.
- 17. Use according to Claim 15 or 16 of compounds of the formula I for the preparation of a medicament for the treatment of diseases caused, mediated and/or propagated by Raf kinases.
- Use according to Claim 17, where the Raf kinase is selected from the
 group consisting of A-Raf, B-Raf and Raf-1.
 - 19. Use according to Claim 18, where the diseases are selected from the group of hyperproliferative and non-hyperproliferative diseases.
 - 20. Use according to Claim 17 or 19, where the disease is cancer.
 - Use according to Claim 17 or 19, where the disease is non-cancerous.

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22. Use according to Claim 17, 19 or 21, where the non-cancerous diseases are selected from the group consisting of psoriasis, arthritis, inflammation, endometriosis, scarring, Heliobacter pylori infection, influenza A, benign prostate hyperplasia, immunological diseases,

autoimmune diseases and immunodeficiency diseases.

- Use according to one of Claims 17, 19 or 20, where the diseases are selected from the group consisting of melanoma, brain cancer, lung cancer, squamous epithelium cancer, bladder cancer, stomach cancer, pancreatic cancer, liver cancer, kidney cancer, colorectal cancer, breast cancer, head cancer, neck cancer, oesophageal cancer, gynaecological cancer, ovarian cancer, cervical cancer, prostate cancer, thyroid cancer, lymphoma, chronic leukaemia and acute leukaemia.
- 24. Use according to one of Claims 15-18, where the diseases are selected from the group arthritis, restenosis; fibrotic disorders; disorders mesangial cell proliferation, diabetic nephropathy, malignant nephrosclerosis, thrombotic microangiopathy syndromes, organ transplant rejection, glomerulopathies, metabolic disorders, inflammation, solid tumours, rheumatic arthritis, diabetic neuropathy and neurodegenerative diseases.
 - 25. Use according to one of Claims 15-18, where the diseases are selected from the group rheumatoid arthritis, inflammation, autoimmune disease, chronic obstructive pulmonary disease, asthma, irritable bowel, fibrosis, atherosclerosis, restenosis, vascular disease, cardiovascular disease, inflammation, kidney disease and angiogenesis disorders.
 - 26. Intermediate compounds of the formula I-1

in which

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Ar denotes phenyl, naphthyl, biphenyl or Het, each of which is 10 unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by R¹.

> Χ denotes -O-, -S-, -(CH₂)_n-, -C(=O)-, -CH(OH)-, -(CH₂)_nO-, $-O(CH_2)_{n^-}$, $-(CH_2)_nS_-$, $-S(CH_2)_{n^-}$, $-(CH_2)_nNH_-$, $-NH(CH_2)_{n^-}$, -(CH₂)_nNA-, -NA(CH₂)_n-, -CHHal- or -C(Hal)₂-,

R denotes H or A,

Het denotes a mono- or bicyclic aromatic heterocycle having 1 to 4 N, O and/or S atoms,

 R^1 denotes A, Ar', OR³, SR³, OAr', SAr', N(R³)₂, NHAr', Hal. NO_2 , CN, $(CH_2)_mCOOR^3$, $(CH_2)_mCON(R^3)_2$, COR^3 , $S(O)_mA$, S(O)mAr', NHCOA, NHCOAr', NHSO2A, NHSO2Ar' or $SO_2N(R^3)_2$

 R^3 denotes H, A or -(CH₂)_nAr'-.

Ar' denotes phenyl which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by A, Ph, OH, OA, SH, SA, OPh, SPh, NH₂, NHA, NA₂, NHPh, Hal, NO₂, CN, (CH₂)_mCOOH, (CH₂)_mCOOA, (CH₂)_mCONH₂, (CH₂)_mCONHA, CHO, COA, S(O)_mA, S(O)_mPh, NHCOA, NHCOPh, NHSO₂A.

NHSO₂Ph or SO₂NH₂,

Ph denotes phenyl which is unsubstituted or mono-, di- or trisubstituted by A, Hal, CN, COOR, COOH, NH₂, NO₂, OH or OA,

Α denotes alkyl having 1 to 10 C atoms, in which, in addition, 1-7 H atoms may be replaced by F and/or chlorine, Hal denotes F, CI, Br or I, denotes 0, 1, 2 or 3, n 5 denotes 0, 1 or 2, m and solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios. 10 27. Intermediate compounds according to Claim 26 in which Χ denotes O, Ar denotes Het which is unsubstituted or mono-, di- or trisubstituted by R¹,

> R denotes H or A, R^1

denotes (CH₂)_mCONH₂, (CH₂)_mCONHA or (CH₂)_mCONA₂,

Het denotes a monocyclic aromatic heterocycle having 1 to 3 N, O and/or S atoms,

and solvates, salts and stereoisomers thereof, including mixtures

thereof in all ratios.

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